The origin of mammalian endothermy: a paradigm for the evolution of complex biological structure

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Several mutually incompatible theories exist about how and why endothermy evolved in mammals and birds. Some take the primary function to have been thermoregulation, selected for one adaptive purpose or another. Others take the high aerobic metabolic rate to have been primary. None of these theories is incontrovertibly supported by evidence, either from the fossil record of the synapsid amniotes or from observations and experiments on modern organisms. Furthermore, all are underpinned by the tacit assumption that endothermy must have evolved in a stepwise pattern, with an initial adaptive function followed only later by the addition of further functions. It is argued that this assumption is unrealistic and that the evolution of endothermy can be explained by the correlated progression model. Each structure and function associated with endothermy evolved a small increment at a time, in loose linkage with all the others evolving similarly. The result is that the sequence of organisms maintained functional integration throughout, and no one of the functions of endothermy was ever paramount over the others. The correlated progression model is tested by the nature of the integration between the parts as seen in living mammals, by computer simulations of the evolution of complex, multifunctional, multifactorial biological systems, and by reference to the synapsid fossil record, which is fully compatible with the model. There are several potentially important implications to be drawn from this example concerning the study of the evolution of complex structure and the new higher taxa that manifest it. © 2006 The Linnean Society of London, *Zoological Journal of the Linnean Society*, 2006, **147**, 473–488.

ADDITIONAL KEYWORDS: correlated progression – megaevolution – origin of mammals – Synapsida – Therapsida.

INTRODUCTION

Nothing is more fundamental for understanding the biological nature of birds and mammals than their endothermic temperature physiology: for organisms to pay the price of some ten-fold increase in their daily food requirements it must be balanced by a very substantial benefit indeed to their ultimate reproductive potential. It is little wonder therefore that a great deal of attention has been paid to the problem of why, how and when endothermy arose. What is rather more surprising is how little agreement there is. At least six different hypotheses currently exist (Hayes & Garland, 1995; Kemp, 2005). There is relatively little fossil evidence available that bears helpfully on the details of the origin of the avian version of endothermy (Ruben, 1995; Schweitzer & Marshall, 2001), beyond

the possession of feather impressions in certain dinosaurs, which is taken to indicate that such forms were already endothermic (Seebacher, 2003; Xu *et al.*, 2004). However, in the case of the evolution of the mammalian version of endothermy there exists the celebrated fossil record of basal Synapsida, or 'mammal-like reptiles', which includes a series of grades of organisms ranging from the indisputably ectothermic pelycosaurs through intermediate levels to the equally indisputably endothermic early mammals (Bennett & Ruben, 1986; Kemp, 2005). The preserved anatomy of these fossils has been extensively scrutinized for support by authors of various of the respective interpretations of the origin of endothermy, although again with little mutual agreement on what structures, if any, are reliable indicators of the nature of the animal's temperature physiology.

The number of contradictory explanations for the origin of endothermy in mammals may in large part be

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due to this scarcity of direct evidence. More fundamentally, it also points to the possibility that these considerations are hampered by a mistaken implicit assumption concerning the evolution of complex structures and associated functions in organisms. As will be discussed later, a more fruitful approach is to pay more than the usual lip service to the presumption that an evolving lineage of organisms must necessarily maintain functional integration throughout its history. The concept of 'correlated progression' (see Kemp, 1999) seems to be widely accepted in principle (e.g. Lee & Doughty, 1997; Budd, 1998), but largely ignored in practice when discussing major evolutionary transitions to new higher taxa. Before taking up this issue, the biological nature of endothermy must be clarified, and the menu of current theories purporting to explain its origin in mammals briefly reviewed.

THE PHYSIOLOGY OF ENDOTHERMY IN LIVING MAMMALS

Typical endothermic temperature physiology of mammals is characterized by four measurable aspects:

1. The basal or resting metabolic rate (BMR) is high. It varies typically from five to as much as ten times that of an ectotherm of similar body size (e.g. Hayes & Garland, 1995; Hulbert & Else, 2000).
2. The body temperature (T_b) is higher than the animal's normal ambient temperature, and lies between about 28 °C and about 40 °C depending on species (e.g. Crompton, Taylor & Jagger, 1978; Eisenberg, 1981).
3. The core body temperature is maintained at a remarkably constant value, not normally varying by more than 1–2 °C over the 24-h diurnal cycle (e.g. Eisenberg, 1981).
4. The maximum aerobic metabolic rate (MAMR) that the organism is capable of sustaining is greatly elevated over that of ectotherms. There is a very approximately constant ratio of 10–15 between the basal rate and the maximum aerobic rate in amniotes, and therefore, like the BMR, the MAMR of an endotherm is typically somewhere between five and ten times that of an ectotherm of similar body size (e.g. Taylor *et al.*, 1987; Hinds *et al.*, 1992; Hayes & Garland, 1995).

Disentangling which of these aspects are the functions and which are the mechanisms responsible for the functions seems clear now, although for many decades there was considerable confusion. The elevated BMR cannot be considered to be of direct functional importance because it is very variable among otherwise similar and closely related species. To name but one of many examples, the study of Shkolnik (1980) showed that the desert-adapted African hedgehog *Paraechinus*

aethiopicus has a BMR only half, and the semi-arid adapted *Hemiechinus auritus* only three-quarters that of the temperate-adapted European hedgehog *Erinaceus europeaus*, yet all maintain the same body temperature of 34 °C, and have similar activity levels. The elevated body temperature also cannot be regarded as an adaptation *per se*, because it too is very variable among otherwise comparable mammal species, and because many ectothermic amniotes operate with body temperatures as high as, or higher than, those of mammals. This leaves two basic direct functions of the endothermic physiological system, thermoregulation and elevated aerobic activity levels, respectively.

THERMOREGULATION

Maintaining a constant body temperature is an ecological adaptation for remaining active over a wider range of ambient temperature. Although in principle this includes high ambient temperatures, the effect is perhaps more striking at the low ambient temperature of night-time. Thermoregulation also serves another, distinctly physiological function. Maintenance of a precisely constant internal temperature is an essential prerequisite for the higher degree of organizational complexity of endotherms compared with ectotherms. The rates of enzyme-controlled metabolic pathways, diffusion rates such as that of transmitter molecules across synapses, and the viscosity and therefore speed of contraction of muscle fibres such as the heart muscle are all temperature dependent, and therefore can only occur at the reliably predictable rates necessary for sustaining the integrity of a complex system if the body temperature is maintained constant. Given the degree of sensitivity of the greatly enlarged and complex mammalian brain to induced temperature changes, it is evident that the central nervous system more than anything depends critically for its proper functioning on maintenance of the correct temperature.

As recently reviewed in the context of the origin of avian endothermy (Schweitzer & Marshall, 2001), the biochemical basis for the elevated BMR lies in an increased number of mitochondria in the cells, mostly those of the visceral organs. They metabolize aerobically and inefficiently, with a consequent increase in heat production (Hulbert & Else, 1989, 1990, 2000). For this to be linked efficiently to a thermoregulatory function requires first that the body is sufficiently well insulated for the body temperature to rise high enough to create a heat gradient between the body and the outside world: the surface conductance has to be low enough. But secondly, there must be a means of varying the conductance of the surface with great speed and precision so that the rate of heat loss can be rapidly adjusted to changes in the net rate of heat input, which

is the sum of the BMR and any heat of activity being generated by muscular exercise. Variable insulation of the skin by variable piloerection, variable blood flow through the cutaneous capillaries and variable posture are the well-known mechanisms for achieving this rapidly adjustable rate of conductance of heat from the body. Many other features such as a more effective circulatory system for heat distribution and a higher oxygen-carrying capacity of the haemoglobin are also necessary, as will be discussed later.

HIGH AEROBIC ACTIVITY

Within the thermo-neutral zone of ambient temperature, much the greater proportion of the additional metabolism above BMR is devoted to muscular activity, and therefore the five-fold or more increase in the maximum sustainable level of aerobic metabolism in endotherms potentially impacts on all the activities of the animal. For example, Bennett & Ruben (1979) quoted a maximum sustainable speed of a 1-kg *Iguana* as 0.5 km h^{-1} and of a mammal of similar body weight as 4.1 km h^{-1}; Farmer (2000) quoted the huge daily locomotory investment in birds foraging for their nestlings. The mechanism behind the raised MAMR is quite simple. A larger number of mitochondria with a larger net membrane area in the muscle tissue, coupled with adequate oxygen delivery by the vascular system, permits a greater rate of ATP synthesis and its conversion to mechanical energy.

The relationship between the increased level of maximum aerobic activity and the thermoregulatory function is poorly understood: the main site of metabolism for thermoregulation is the viscera, that for aerobic activity is the musculature, but there is no obvious mechanical or functional reason why they should be linked to one another (Bennett & Ruben, 1979). Nevertheless, a considerable body of empirical evidence in living organisms demonstrates the roughly constant ratio between the two values in both ectotherms and endotherms (e.g. Bennett & Ruben, 1979; Hayes & Garland, 1995; Ruben, 1995; Krosniunas & Gerstner, 2003). Suggestions of possible reasons for the correlation include: a relationship between an increase in the metabolic activity of the muscle tissue and a corresponding increase in the metabolic functions of the viscera necessary to maintain the muscle tissue (Ruben, 1995); a coincidental correlation between a raised BMR for maintaining a higher incubation temperature for the juvenile and an increased need for higher muscle activity levels associated with food collection for provisioning the young (Farmer, 2000); a correlation between increased locomotory activity for food collecting and increased visceral metabolism for assimilation of the extra food (Koteja, 2000); and a requirement that the BMR remains a constant fraction of the MAMR in order to maintain a rapidly increased oxygen supply via the circulatory system during high activity levels (Krosniunas & Gerstner, 2003). This problem will be returned to.

CURRENT THEORIES OF THE ORIGIN OF ENDOTHERMY

The lack of an explicit reason for a relationship between the physiology of thermoregulation on the one hand and of aerobic capacity on the other has led to a taxonomy of theories that divides them into two categories, the 'thermoregulation first' and the 'aerobic capacity first' views. Within each of these there are differences in what is hypothesized to have been the initial selective pressure promoting the evolutionary progress towards endothermy.

THERMOREGULATION FIRST – PHYSIOLOGICAL VERSION

The most detailed version of several claims that endothermy arose initially for the benefit that a constant body temperature endows on the physiological integration of the organism is McNab's (1978) theory of miniaturization. He envisaged that the synapsids originated from small-bodied ectotherms. They then evolved increased body size, up to 30–100 kg, at which point they became inertial homeotherms, the condition where the animal is buffered by its low surface area to volume ratio against short-term fluctuations in the ambient temperature. Insulation in the form of a pelt may have been acquired at this stage to enhance the effect. Therefore, the body temperature remained close to constant, with the consequent benefits of constant rates of enzyme activity, nerve conduction rates, etc. The second step was a process of reduction in body size, but in order to retain the constancy of the body temperature there had to be a relative increase in metabolic heat production, and in insulation. This evolutionary sequence was represented by successively smaller non-mammalian cynodonts, and culminated in the very small body mass of the first mammals, which had a body weight of the order of 10–20 g.

McNab (1978) claimed that the actual body sizes seen in the fossil record support his theory, with the small ectotherms represented by basal amniotes ('cotylosaurs'), and the inertial homeotherm stage represented by large-bodied Late Carboniferous and Early Permian pelycosaurs and the Late Permian basal therapsid taxon Pristerognathidae. This is followed by reduction in size in the sequence of Triassic cynodonts. As well as becoming smaller in body size, the cynodont sequence also exhibits the evolution of a secondary palate, indicating an increase in ventilation rate and by implication of metabolic rate. Unfortunately, the phylogeny of therapsids adopted by McNab was

pre-cladistic and is now grossly out of date. The widely accepted modern version (Hopson, 1991; Kemp, 2005) offers no support at all to his argument. In the first place, there are medium- and small-bodied pelycosaurs, as well as the large-bodied ones, throughout their history (Reisz, 1986); in the second place, the pristerognathids are now regarded as part of a monophyletic Therocephalia, which is the sister group of cynodonts plus mammals, and which includes a considerable size range of members with skull lengths ranging from 30 cm to less than 10 cm. Cladistic analysis of the fossils implies that the common ancestor of cynodonts and therocephalians was in fact a relatively small-bodied form. In the third place, the cynodonts also embrace a wide size range. There are small-bodied forms dating from the Early Triassic such as *Thrinaxodon* and *Galesaurus*, and from the Middle Triassic such as *Probainognathus*, skull lengths of which are approximately 7 cm. But there are also large bodied Early, Middle and Late Triassic forms, with skull lengths ranging around 30 cm, for instance *Cynognathus* and *Exaeretodon*. Yet, small-, medium- and large-bodied alike, these cynodont-grade therapsids all possess the same characteristics such as a fully differentiated dentition, enlarged and reorganized jaw musculature, a secondary palate, reduced lumbar ribs and a mammal-like hindlimb. In so far as features such as these are presumed to be correlated with metabolic rate, the similarity implies that they all possessed a comparable temperature physiology irrespective of body size. Only the final stage in the transition from cynodont-grade to Mammalia, which occurred in a single Late Triassic lineage, corresponds to the expectations of McNab's theory: all the earliest mammals were indeed small.

Bennett, Hicks & Cullum (2000) attempted to refute experimentally this, or any other theory which proposes that a rise in metabolic rate immediately endows a degree of thermoregulation. They gave lizards a very large meal, which has the effect of increasing the metabolic rate of the viscera by 3–4 times, presumably to increase the rate of digestion. The authors then tested for an enhanced thermoregulatory ability, but found no significant increase in the body temperature or decrease in rate of cooling, compared with the control lizards that had not been force fed.

THERMOREGULATION FIRST – BRAIN SIZE VERSION

Hulbert (1980) pointed out that 5–10% of the BMR of a mammal is due to the metabolic activity of the brain, and that therefore selection for an enlarged brain of itself may in part have led to endothermy. In fact, the relationship between brain size and BMR across species does not support such a simple interpretation (Harvey & Krebs, 1990; Harvey & Pagel, 1991).

However, it may be the case that the evolution of thermoregulatory ability was itself necessary for the evolution of the large, complex brain of endotherms, typically ten times the size of that of ectotherms. Certainly the functioning of the mammalian (and avian) brain today depends on precise control of the internal environment of the body including temperature (Jerison, 1971; Allman, 2000). Evidence from the fossil record concerning synapsid brain size is ambiguous because it was not until the mammals themselves that the brain actually filled the cranial cavity, permitting accurate estimates of its size. Indeed, the basal cynodont brain has been reconstructed on the one hand as significantly increased in size (Kemp, 1979), and on the other as scarcely enlarged beyond the range seen in living reptiles (Hopson, 1979; Rowe, 1996). If the former estimate is accepted, then enlargement of the brain coincided with the evolution of the cynodont features frequently associated with an increased metabolic rate and the beginning of endothermy.

THERMOREGULATION FIRST – ECOLOGICAL VERSION

The theory that the initial function of endothermy was maintenance of a constant body temperature so that the organism could be active at night has been promulgated most cogently by Crompton *et al.* (1978) and Taylor (1980). By their calculations, a small animal that is well enough insulated by fur can maintain a constant body temperature with little or no increase in BMR, provided that the ambient temperature is low enough. They argued that this was indeed the case in the ancestral mammals, where a virtually reptilian-level metabolic rate would have been adequate to maintain a constant body temperature of between 25 and 30 °C at the ambient temperatures prevailing at night. The ability of most modern mammals to remain active during the day requires a higher body temperature in order to have the ability to lose heat fast enough; this in turn requires a higher BMR to generate it. Therefore, the shift to diurnality was presumed to be a secondary stage, not found until the post dinosaur radiation of mammals in the Cenozoic.

Evidence for the theory is two-fold. There are several groups of living nocturnal mammals, notably tenrecs, hedgehogs and small marsupials, with relatively low body temperatures and metabolic rates. Crompton *et al.* (1978) claimed that these had retained the ancestral mammalian condition. In fact, the distance of the relationships between this very disparate sample of mammals makes such an inference exceedingly unparsimonious, and all are surely secondarily modified independently of one another. Nevertheless, the very existence of mammals with such physiological characteristics, even if specialized among today's mammals, indicates that the theory is feasible. The

second line of evidence is that the earliest mammals show several signs of having indeed been nocturnal. The small body sizes, agile skeletons and insectivore-adapted shearing molar teeth all point to a close analogy in life style with modern insectivorous mammals, which are primarily nocturnal in habit. The evidence for increased acuity of hearing as indicated by the evolution of the ear ossicles, and even more so of olfaction as indicated by the development of the neocortex in the primitively olfactory telencephalon region of the brain, both imply nocturnal rather than diurnal hunting, in which vision would be expected to dominate.

However, there are arguments against this nocturnalization theory. The most important is that it implies that there was no increase in metabolic rate in cynodonts and early mammals, despite all the morphological features found in these fossil forms that apparently indicate an enhanced metabolic rate. These include the presence of a secondary palate, and the remodelling of the rib cage to the morphology associated in living mammals with a functioning diaphragm, both of which are indicative of a higher ventilation capacity. The modification of the dentition, mandibular anatomy and jaw musculature, which together permit forceful but precise tooth occlusion, is hard to interpret in any way other than as an adaptation for increased rate of food assimilation. The virtually mammalian organization of the postcranial skeleton points to the existence of high levels of locomotory activity, at least facultatively.

Experimental testing of the general idea that insulation alone can endow an ectotherm with endothermic abilities was provided by Cowles (1958), by covering a lizard with a mink fur coat and assessing its thermoregulatory ability. He reported that, as expected under the laws of simple physics, there was a decrease in the rate of warming of the specimen when it was removed from cold to hot conditions, and of cooling when placed back into cool conditions. However, as Cowles himself cautions, it is not clear how reliable an indicator of an actual evolutionary transition such an observation is. A modern ectotherm's skin and its associated vascularization is primarily designed as a heat-absorbing surface, whereas the external surface of an endotherm is adapted for differential heat loss, under the control of neuronal and endocrine mechanisms absent from reptiles.

THERMOREGULATION FIRST – GROWTH OF OFFSPRING VERSION

Farmer (2000, 2003) speculated that the initial selection pressure for the evolution of endothermy was for increased parental ability to maintain a higher incubation temperature for the developing young. The argument is based mainly on observations regarding the sensitivity of vertebrate embryos generally to their ambient temperature, from the point of view of both avoiding developmental abnormalities and increasing the rate of development, a generality disputed by Angilletta & Sears (2003). Furthermore, the dual role of thyroid hormones in reproduction and in the control of metabolic rate suggested to Farmer a possible mechanism for the initial evolution of the enhanced BMR. In this particular theory, the increase in maximum aerobic activity in endotherms may have evolved subsequently as a further manifestation of parental care, namely to increase the rate of food collecting to nourish the young. No fossil evidence is quoted.

AEROBIC CAPACITY FIRST – SUSTAINED ACTIVITY VERSION

The theory that selection acted initially to increase the MAMR was first explicated in detail by Bennett & Ruben (1979, 1986) and Ruben (1995) in their 'aerobic capacity' model, and is one of the most influential explanations for the origin of endothermy. Asserting that a small increment in BMR in the absence of associated insulation would have a negligible effect on thermoregulatory ability, they proposed that the initial selection for endothermy was to increase aerobic scope: even a small incremental increase in the maximum sustainable aerobic level of activity would be expected to have had an immediate impact on the life of the animal.

Actual evidence for the aerobic capacity theory comes from the observation that the basal and maximum aerobic metabolic rates are decoupled from one another to the extent that the former is due mainly to the metabolism of the tissues of the visceral organs while the latter is due mainly to that of the musculature. Therefore, it is inferred that the two functions evolved independently, and because selection could not have been for thermoregulation initially, it must have been for increased sustainable aerobic activity level of the muscles. However, due to the correlation that exists between BMR and MAMR, the BMR also increased and this paved the way for the appearance of thermoregulation at a later stage in the evolution of fully developed endothermy. A number of authors have proposed that a demonstration of a significant correlation between BMR and MAMR in living animals constitutes a test of the aerobic capacity theory (e.g. Hayes & Garland, 1995; Dohm, Hayes & Garland, 2001; Boily, 2002; Gomes *et al.*, 2004). Interesting and important for understanding the origin of endothermy as this issue is, strictly speaking the aerobic capacity theory does not require that there has to be a correlation between the two rates, but only that increased activity level could evolve prior to, and independently
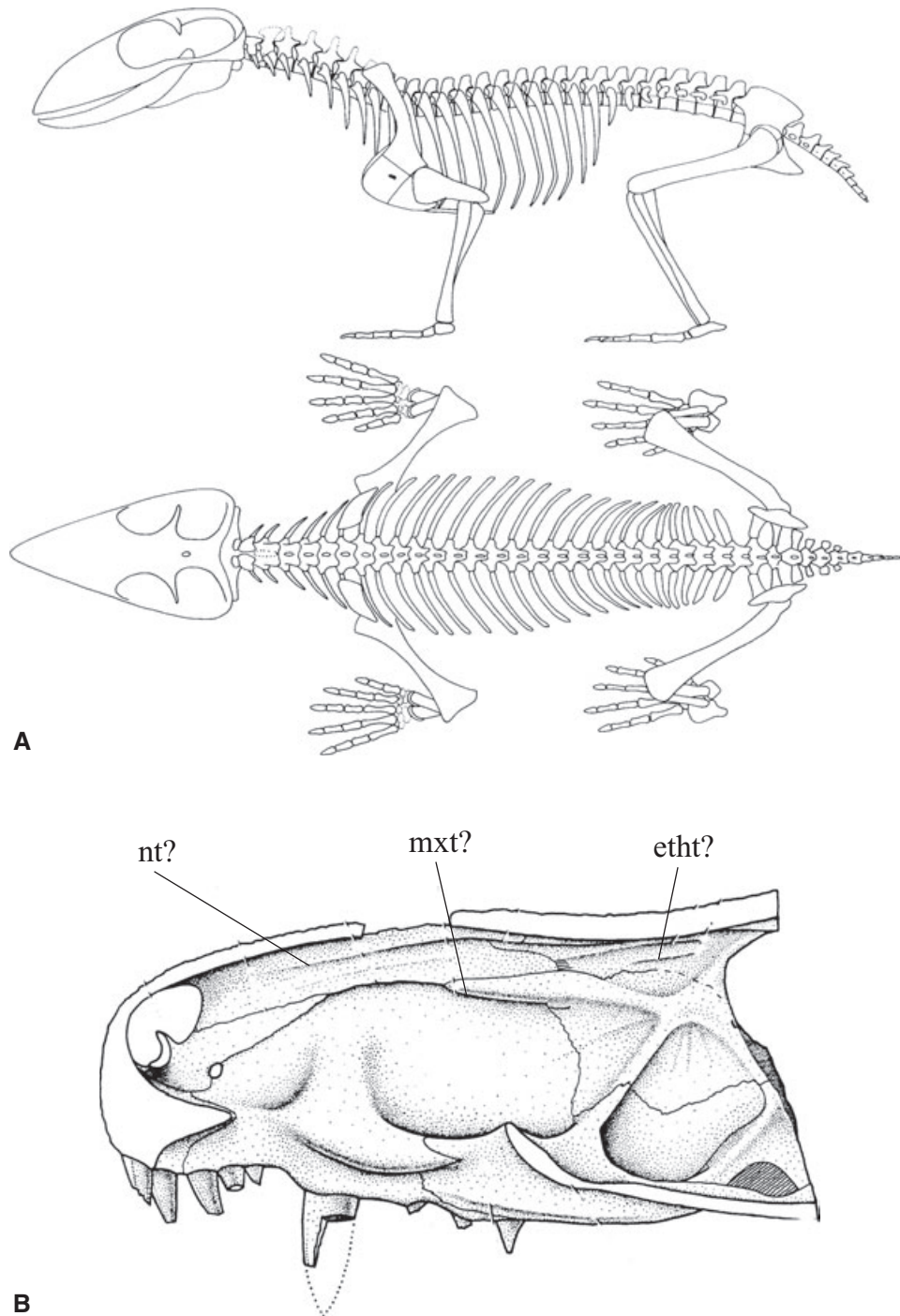
Figure 1. A, reconstruction of the skeleton of the therocephalian therapsid *Regisaurus* in lateral and dorsal views (from Kemp, 1986). B, internal view of the nasal cavity of the therocephalian *Glanosuchus* (from Hillenius, 1994). Abbreviations: etht?, possible ethmo-turbinal ridge; mxt?, possible maxillo-turbinal ridge; nt?, possible naso-turbinal ridge.

of, thermoregulation, whatever the nature of the mechanisms underlying the two respective functions.

Evidence from the fossil record has also been claimed to support this theory, by demonstrating the occurrence of levels of increased aerobic activity in therapsids that are otherwise very primitive compared with mammals (Bennett & Ruben, 1986). The modification of the locomotory system in basal ther-

apsids (Fig. 1A) was interpreted by Carrier (1987) as a means of increasing the ventilation capacity. Getting rid of lateral undulation of the vertebral column, raising the body permanently off the ground by repositioning the limbs so that the feet lie closer to the mid-line, and reducing the lumbar ribs all suggest that a diaphragm had evolved, to complement costal breathing during times of high activity, when increased oxygen was required if aerobic activity was to be sustained. Reasonable as this interpretation of the evolution of the postcranial skeleton is, it may be incomplete in so far as there are additional possible explanations for the change in limb posture in therapsids, notably increased acceleration and agility (Kemp, 1982). These attributes of locomotion do not necessarily correlate with high levels of aerobic activity, as may be true in the case of the facultatively erect gait of crocodiles. In any case, demonstration of elevated levels of aerobic locomotory activity in therapsids would not necessarily exclude the possibility that thermoregulation was also present.

The second fossil evidence cited is the interpretation of certain fine ridges on the inner surface of the nasal cavity found in the therocephalian *Glanosuchus* (Fig. 1B) as the site of attachment of maxillo-turbinals (Hillenius, 1992, 1994; Ruben, 1995), which serve to humidify and warm the inspired air in mammals. The absence of the actual turbinal bones is presumed to be due to either their cartilaginous or their very delicate osseous nature. However, the supposed maxillo-turbinal ridges are very small, and could equally well be the sites of turbinals associated with olfactory epithelium. Furthermore, their presence is highly inconsistent in therapsids. There are various ridges in the nasal cavity of gorgonopsians (Kemp, 1969) but all lie above or behind the path of the inspired air. Similarly the dicynodont *Oudenodon baini* (my pers. observ.) lacks evidence for a suitably positioned maxillo-turbinal. Sigurdsen (unpubl. data) recently sectioned a snout of a therocephalian and did not find the specific ridge described for *Glanosuchus*. The basal cynodont *Procynosuchus* has turbinal ridges on the dorsal surface of the nasal cavity, but no trace on the lateral surface, where a maxillo-turbinal would be expected (Kemp, 1979). Again it should be pointed out that if indeed present, maxillo-turbinals would be just as consistent with other views on the origin of endothermy as with the aerobic capacity first theory.

AEROBIC CAPACITY FIRST – JUVENILE PROVISION VERSION

Koteja (2000) proposed what he termed the 'assimilation capacity model'. The primary selective force involved was intensified parental provisioning of the juveniles, presumably in the form of food initially, but subsequently in the case of mammals as lactation. Increased daily energy expenditure was required for the enhanced locomotory efforts devoted to food collection. An increase in the metabolic activity of the visceral organs was also required, to assimilate the increased food intake by the parent. Thermoregulation was not initially a part of the selective regime, but evolved later as a side-effect of the leakiness of the plasma membranes that inevitably accompanied the increased metabolic rate. By his own admission, feasible as it might be, Koteja's theory is virtually untestable, either from the fossil record or from comparative studies of living endotherms.

AN INTEGRATED VIEW OF THE ORIGIN OF ENDOTHERMY

Why has the problem of the origin of endothermy failed to be solved to general satisfaction? In the first place, it is because the available empirical evidence is very limited and invariably ambiguous. Morphological features of fossils claimed to be associated with a particular mode of thermal physiology are always open to alternative interpretations, such as the possible function of a secondary palate in mastication, complex dentition for a specialist rather than simply abundant diet, and the reorganization of the postcranial skeleton for agility. There does appear to be a relationship between bone histology and growth rates, although it is far from clear how this in turn might be related to metabolic rates (e.g. Horner, de Ricqles & Padian, 1999; Botha & Chinsamy, 2000; Ray, Botha & Chinsamy, 2004). Predator–prey ratios, although sometimes proposed as an indicator of the high levels of food requirements of endotherms, have been dismissed as too unreliable (Bennett & Ruben, 1986). Living amniotes are no more helpful than fossils. The various 'subendothermic' modern mammals can readily be shown by cladistic analysis to be secondarily specialized rather than relics of earlier evolutionary stages: neither daily torpor in bats, nor low metabolic rates of desert hedgehogs, nor the virtually ectothermic nature of the naked mole rat are reliable indicators of actual ancestral grades. Attempts to illustrate steps in the evolution of endothermy by simple experimental manipulations of modern animals inevitably ignore the very complexity of the system that is being addressed: the reaction to artificial fur coats or large, force-fed meals by ectotherms that otherwise possess none of the subtle complex of regulatory devices of endotherms are unlikely to illuminate realistic intermediate stages.

However, there is a second and more fundamental reason for the continuing dispute about the origin of endothermy, which is that the majority of authors of, and commentators on, the respective current theories

subscribe to the assumption that all the physiological mechanisms and ecological consequences of modern endothermy could not possibly have evolved at the same time. Therefore, the implicit argument continues: there must have been a temporal sequence starting with selection for a single, primary function, to be followed only later by selection for secondary functions and the further structures associated with them. What the respective authors seek is the most feasible reconstruction of this presumed sequence, supported by arguments of such dubious merit as '*It seems unlikely* that small endotherms could evolve directly from small ectotherms because the low rates of metabolism and high conductances typical of ectotherms must be converted to the very high rates and low conductances of small endotherms.' (McNab, 1978: 4), or '*It is difficult to conceive of* these metabolic increments occurring for strictly thermoregulatory purposes, particularly at the initial stages of the evolution of endothermy when they would have been ineffective in establishing thermostability.' (Bennett & Ruben, 1979: 650) [emphasis added].

A few authors have considered the origin of endothermy from a more integrated point of view. Kemp (1982, 2005) presented a flow-diagram indicating how the various structures and functions of mammals, including those associated with endothermy, are related to one another in the integrated organism, and how this constrains theories about the origin of mammalian biology in general. Koteja (2000) presented a much more limited but logically similar scenario, focused on the effect different aspects of endothermic physiology might have on postnatal care. In a particularly illuminating review of the origin of avian endothermy, Schweitzer & Marshall (2001) recognized that a large number of correlated characteristics had to change to achieve full endothermy. Their particular model begins with a molecular mutation increasing the oxygen affinity of haemoglobin and includes subsequent changes in mitochondria, ventilatory and musculo-skeletal systems, insulation and reproductive strategy.

There are good grounds for starting with different fundamental assumptions about how complex biological systems and the new higher taxa that express them evolve. Together these constitute the long-introduced but in practice largely ignored correlated progression model of the origin of new higher taxa, or megaevolution (see Kemp, 1985, 1999). The assumptions of the correlated progression model may be stated thus:

1. The characteristics of an organism are highly integrated with one another, so that no single one of them can evolve by more than a small increment at any one time without losing its functional integration within the organism as a whole.

2. Natural selection tests the fitness of an organism as a whole, not of any of its individual characteristics.
3. Therefore, over the course of the evolution of new complex structure, including the broad biological reorganization associated with the origin of a new higher taxon, all the structures and associated functions must evolve by respective sequences of small steps in loose correlation with each other in order to maintain continuous functional integration.

Under this model, explaining the course of evolution of any particular case of megaevolution, such as the origin of endotherms, becomes a matter of understanding the nature of the integration between all the structures and functions involved in the evolutionary transition, rather than identifying one particular structure or function as paramount over the rest as far as selection is concerned. Clearly from this perspective, it is unrealistic to consider even the origin of endothermy alone, because it too cannot be understood in isolation of other structures and functions of the organisms that are not immediately associated with temperature physiology, a point taken up later.

To illustrate in broad terms the concept as applied to the origin of endothermy, imagine, for example, a mutation that resulted in an increased number of mitochondria in all the cells, say by 10%, and consider the effects this might be expected to have (Fig. 2). Assuming that the animal's pulmonary and vascular systems were capable of delivering the extra oxygen required, there would be an instant increase of around 10% in the maximum possible rate of aerobic activity of the muscles, with the effect of increasing the animal's maximum sustainable running speed by a few per cent. An increase of comparable magnitude in the resting heat production by all the tissues would also be expected, and provided the rate of cutaneous blood flow and therefore of conductive heat exchange through the skin was already capable of some control, as it is in living ectotherms, there would immediately exist the capacity for the organism to remain at an active body temperature for a few extra minutes at either end of its working day. Potentially this same increment in internal heat production would also result in a reduction in the amplitude of the daily fluctuation of body temperature, thereby reducing by a few per cent the variance in rates of enzyme activity, and physiological processes such as neurotransmission in brain function. In so far as the organism already had a modicum of parental care, the enhanced activity level and foraging time, and the more stable, elevated body temperature would all contribute to an incremental increase in the level of that care. In short, the hypothesized 10% increase in mitochondrial number would have had an instant incremental effect on all of the functions of endothermy at the same time.
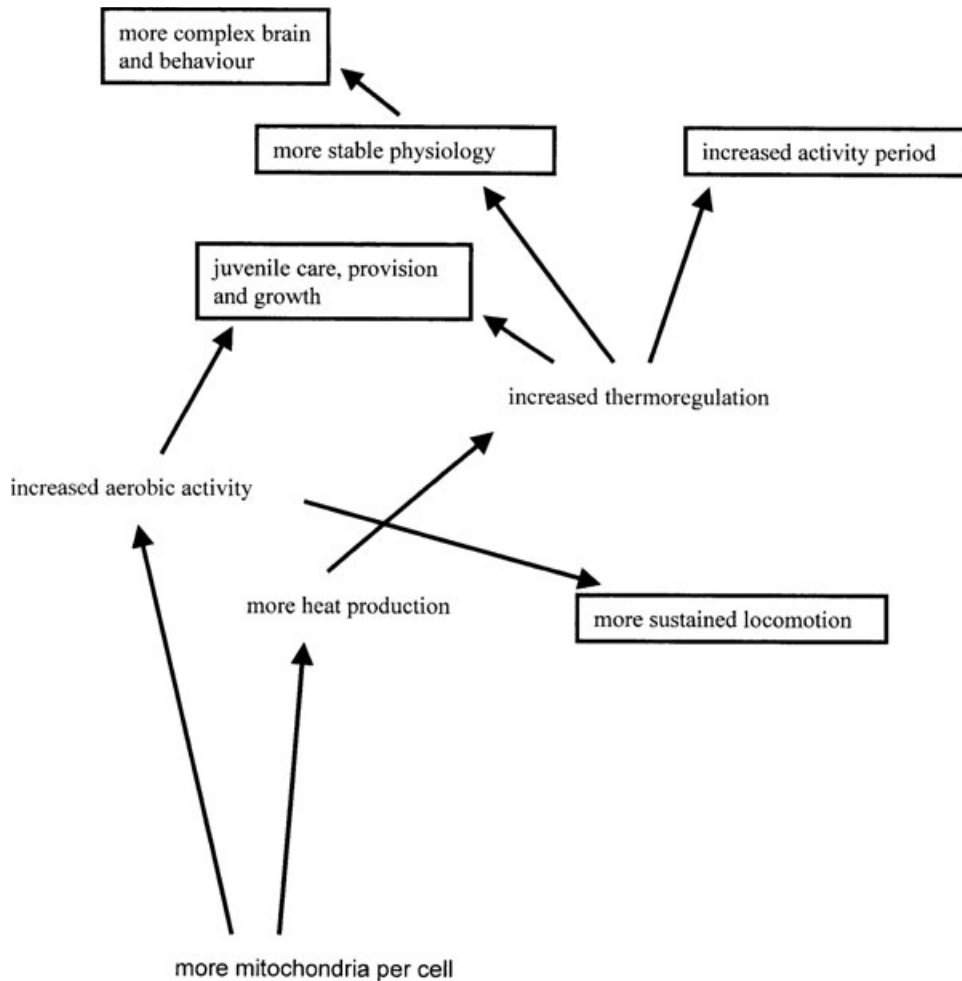
Figure 2. The proposed effect of a small increase in the number of mitochondria per cell on several functions of endothermy.

The consequence for such a hypothetical organism would be a minor shift in several of the dimensions of its niche simultaneously; given the right circumstances, such may well be of selective advantage.

As will be appreciated, the correlated progression hypothesis requires that the nature of the functional interrelationships between the structures and processes involved are such that a small mutational modification in one can be accommodated immediately, by appropriate non-genetic adjustments, in others. Indeed as will be addressed later, this requirement underlies the main test of the hypothesis. For instance, the supposed heritable increase in mitochondrial number could only affect metabolic rates if there was an existing ability of the lungs, heart and arterial system to deliver increased oxygen to the tissues. For the potential functions of the elevated metabolic rate to be manifested, the existing central and peripheral nervous systems must also be able to control the enhanced locomotory activity; the food-collecting and processing systems to acquire the necessary incremental increase in food requirements; the skin to regulate heat flow; and so on. What would happen if one of the functions did not have what might be termed this 'spare functional capacity'? This particular function would now be limiting, and the correlated progression model predicts that a mutation causing it to be suitably modified is necessary before further progress is possible. For example, suppose the limit was imposed by the inability of the ventilation system to acquire enough gaseous oxygen for any higher metabolic rate. Further progress towards endothermy would have to await a mutation that resulted in, say, a larger lung capacity or a higher ventilation rate. Or suppose that the conductivity of the skin proved to be too high for any higher level of metabolic heat to be effectively retained. A mutation causing a decreased conductivity would be awaited, at which point a higher level of heat production would now be viable, thereby enhancing the incipient thermoregulation.
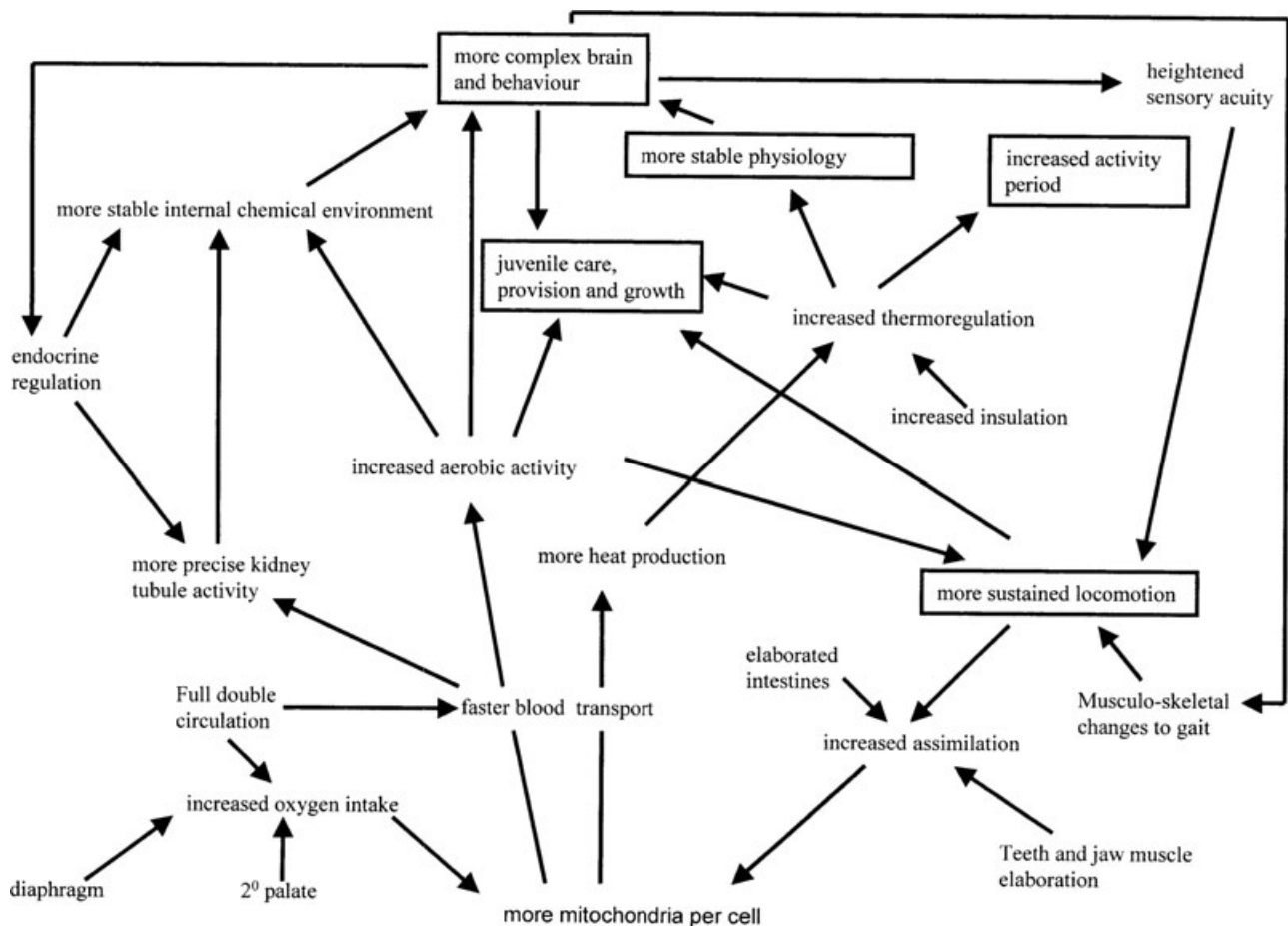
Figure 3. The interrelationships of the structures and functions responsible for or affected by endothermic temperature physiology of a mammal.

Figure 3 illustrates the principle of the evolution of endothermy by correlated progression. All the original proposed functions (in boxes) are now seen to be deeply and inextricably embedded within the complex functioning of the whole. Other structures and functions could readily be added, and of those shown, most represent complex attributes in their own right: as well as fitting congruently into the overall scheme, a character such as 'gait' or 'brain' itself consists of integrated parts. Solely for illustrative purposes, this simple account of how the correlated progression model might work for the origin of endothermy started with a hypothesized increase in the number of mitochondria per cell. In fact any other structure or process could equally well have been chosen to begin with, and the characters could have changed, increment by increment, in virtually any order. The essential point is that only a small change in any one characteristic at any moment in evolutionary time is possible, but the characteristic in question can be one of many. It is neither important nor predictable which one it will be. There will be moments in the evolutionary sequence when one particular feature is critical in the sense that it is limiting the changes in others, but the limit will be duly removed when that feature is itself subject to an appropriate mutational modification.

The theory of the origin of endothermy presented here is that the separately recognizable functions of endothermy in mammals evolved as a single, integrated complex, and that it is meaningless to suppose that any one function was ever primary. Over the time it took, small incremental changes in individual features occurred in parallel, and this produced small, integrated enhancements of all the functions in correlation with one another.

TESTING THE HYPOTHESIS

It is entirely plausible that this interpretation of the process by which the complex, multifunctional characteristic called endothermy arose is correct, but how to test it as a scientific hypothesis may seem problematic. The correlated progression hypothesis predicts that the exact sequence of very small, successive

changes associated with the evolution of fully expressed mammalian endothermy will be far below any possibility of the fossil record to resolve. Nor can evidence from living amniotes reveal the sequence, because the ectotherms show few relevant signs of incipient endothermy, and the mammals all evolved from a common ancestor already possessing full endothermy. What can be done is to apply tests at a lower resolution, in other words to assess whether the correlated progression model is the most realistic general model for accounting for the origin of endothermy. If this proves to be so, then it has to be accepted that seeking a single, specified initial selection force or function for endothermy is in vain. Nor will it be possible to discover a particular sequence of evolutionary steps by which full mammalian endothermy evolved.

There are three kinds of argument or test that do, indeed, support the general correlated progression model: (i) inference from the nature of the integration between the structures and processes associated with endothermy in living amniotes; (ii) inference from computer modelling of how complex systems in general evolve under a selection process; and (iii) demonstration from the fossil record that what relatively little is known about the pattern of acquisition of characters associated with endothermy in mammals is nevertheless more closely compatible with correlated progression than with alternative models.

(I) Integration between structures and processes in living mammals

The model predicts that the quantitative variability in function of virtually all the integrated individual processes is sufficient to allow instant adjustment to the effect of a genetic modification of any one of them. A large, though disconnected, volume of observational and experimental work indicates that the range and pattern of variability in the parameters of temperature physiology are indeed compatible with the required degree of loose functional correlation. There are several categories of such evidence, a few examples of which will illustrate the argument.

Some studies show that appropriate adjustments in existing functions in response to a change in another occur. For example, Hicks & Farmer (1999) used comparative physiological literature and a theoretical analysis to show that the basic reptilian lung structure is capable in principle of supporting the increased oxygen requirements of endothermic physiology; indeed, the oxygen consumption of some modern lizards exceeds that of some living endotherms of the same body weight. Furthermore, the oxygen transport system from lungs to tissues consists of a series of steps, diffusive and convective, that are closely integrated with one another. The partial pressure of oxygen at each stage is dependent on that of the previous stage, suggesting that an increase in transport rate at one point in the system could automatically be accommodated by increases at others.

There is direct evidence, notably in aquatic chelonians (e.g. Jackson & Prange, 1979), concerning the ability of the incompletely divided reptilian heart to adjust its output between virtually complete mixing and virtually complete separation of the systemic and pulmonary flows. This implies that cardiac output could cope immediately with an evolutionarily imposed increased oxygen requirement.

A second relevant category of study of living organisms is comparative. Considering the relationship between metabolic rate and thermoregulatory structures, Shkolnik's (1980) study of hedgehogs from three different habitats referred to earlier showed that although the same body temperature of 34 °C was found in all three, the BMR varied. Furthermore, the conductance value of the skin varied, but in contrast the rate of evaporative loss under hot ambient conditions was approximately the same. In all three species, the values of the parameters coincided with expectations for, respectively, a temperate, a semi-arid and a desert-adapted species of otherwise very similar, closely related mammals. The implication from this and numerous similar cases of small differences in various parameters found in the particular versions of endothermy among various mammals is that different features associated with endothermy can evolve to some extent independently of one another, and yet remain integrated with other features to the extent that the overall temperature physiology of each species is adapted for the particular ambient conditions that its members normally meet.

Another, particularly illuminating illustration of the nature of the correlation between different features is the relationship between the high metabolic rate of the visceral organs that is associated mainly with the high BMR, and that of the muscle tissues associated mainly with the high MAMR. None of the various attempts mentioned earlier to discover a functional connection between them that accounts both for the general correlation and for the variation in the ratio among different species is convincing. The correlated progression model not only explains the connection, but predicts it. The two metabolic rates, BMR and MAMR, evolved as separate features in so far as they are directly associated with the separate respective functions of thermoregulation and increased activity. But, as illustrated in Figure 3, these functions are themselves correlated with one another indirectly because they are related through many other structures and functions, and so they both contribute to the multiple, inextricably intertwined functions of endothermy in the life of the mammal in its habitat. At the

same time, however, the correlation is sufficiently loose that species in different niches with different particular requirements are able to evolve different quantitative values for these parameters.

A third kind of evidence is derived from studies of responses to artificially imposed changes. For example, the mammalian lung has a marked ability to undergo compensatory growth in response to damage, as reviewed recently by Hsia (2004). This indicates how readily a small, phenotypic adjustment to increased oxygen requirements could occur in this particular part of the oxygen transport system. In fact, the entire concept of developmental feedback mechanisms that induce compensatory changes in one system, be it neural, muscular, osteological, enzymatic, etc., in response to a genetically or environmentally induced modification in another – one of the fundamental properties of life – speaks for the correlated progression model.

(II) INFERENCE FROM COMPUTER MODELLING OF HOW COMPLEX BIOLOGICAL SYSTEMS EVOLVE

Niklas (1995, 1997, 2000) used a computer simulation program for evolution by natural selection of hypothetical simple terrestrial plants. He considered the optimal requirements for each of up to four functions in such plants, namely mechanical stability (low or closely spaced branches), light interception (widely spreading branches), water conservation (low plant with few branches) and spore dispersal (multiple high branches). The program was arranged to select at each step the randomly generated variant with the best compromise structure between the conflicting requirements for these functions. The result of the series of runs was a considerable range of morphologies (Fig. 4) which all represent compromise structures that are more or less equally well adapted. Interesting too, the various outcomes were frequently similar in general form to known fossil primitive plants.

The inferences to be drawn from this study are three-fold, and by analogy they point to the correlated progression pattern of evolution. The first is that natural selection is concerned with the total fitness of the organism, as contributed to by all its structures and their functions simultaneously. Perhaps in some single generation one character alone might be critical and therefore variation in that character alone will determine the direction of evolution. But this will be at most a transient stage and normally variation in many characters will contribute to the overall fitness level. The best compromise among the conflicting optima for several discrete functions will be the variant that is selected. The second inference is a corollary of the first. There will be many possible sequences of increasingly well-adapted compromises. The sequence actually followed in a particular case will depend on a variety of contingent circumstances, such as the exact variation available for selection to act on, and the fine details of the environment of the moment (see Mani & Clarke, 1990, for a computer model that makes a vary similar point but at the level of intrapopulation genetics). The third inference is that at any given time, change in many of the characters will not be due to natural selection acting directly on those characters. Rather, these changes will be due to a form of drift as they hitchhike as part of those variant organisms that are selected because they momentarily possess a more favourable overall combination of characters. Indeed, a variant of a character could well survive even
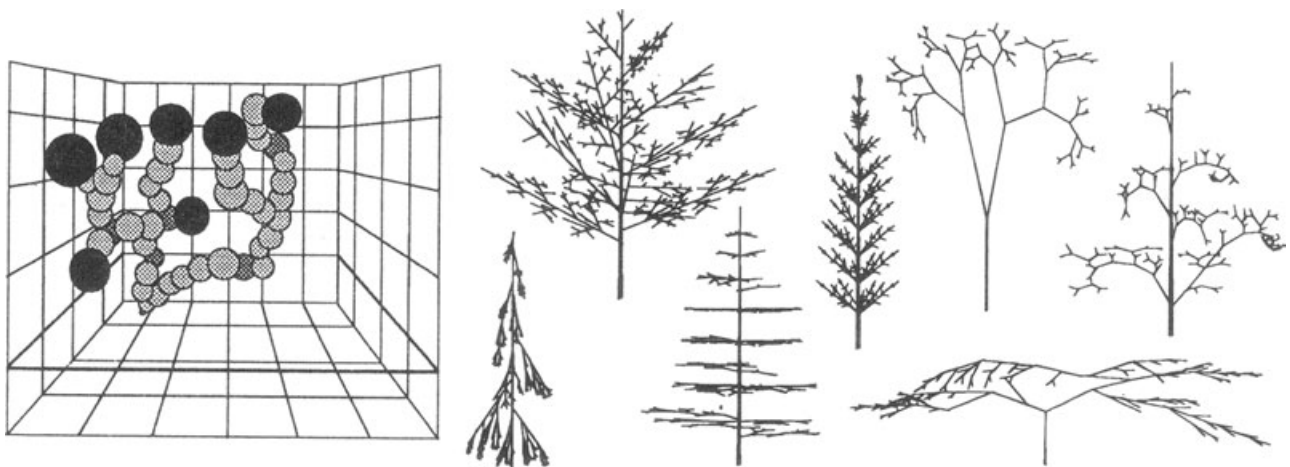

Figure 4. On the left, computer-generated walks through a multi-task landscape requiring adaptation simultaneously for light interception, mechanical stability and reproductive success. On the right, some of the optimal compromise morphologies generated by different walks (from Niklas, 1995).

though it is mildly disadvantageous as far as its particular function is concerned.

Lenski *et al.* (2003) used a logically comparable but much more sophisticated computer program to investigate the evolution of complex characters. It starts with simple, replicating digital 'organisms' but which have the possibility of acquiring certain random 'mutations' (logical functions, in computer terms). Several particular 'mutations' increase the units of 'energy' (computational merit) available to the organism. Complex structure is represented by particular combinations of several such favourable 'mutations', which have ever-greater units of 'energy' available, and which therefore represent ever-greater 'reproductive fitness'. The maximum 'energy' is available to a stage referred to as EQU, which in principle could be achieved by as little as 16 'mutations', as long as they were the right ones appearing in the right order. The actual outcome of the simulations was that of 50 runs, EQU was achieved 26 times, but that the number of 'mutations' occurring in these respective lineages to the point at which EQU arose varied from 51 to 721 steps. The precise sequence of 'mutations' by which EQU was achieved also varied, illustrated starkly by the fact that the final 'mutation' leading to EQU differed from lineage to lineage. In the course of evolution of the lineages, no particular 'mutation' was essential for the subsequent appearance of EQU, and there were cases of 'mutations' that were deleterious when they first arose, or that were involved in a tradeoff with more favourable 'mutations'.

Like the simpler, morphological analogy program of Niklas, here too the pattern of acquisition of characters leading to the evolution of a new complex system that is composed of functionally interrelated parts corresponds to a correlated progression. Selection is concerned with the overall operation of the system rather than its individuated parts, the parts are functionally correlated, and there are so many routes to achieving the same overall level of complexity of function that it is not possible to predict which precise route will be followed. In so far as the evolution of complex biological structure under the influence of natural selection can be expected to follow the same logical rules as these computer simulations, then the correlated progression model is corroborated.

(III) Inference from the sequence of acquisition of characters inferred from the fossil record

Kemp (1982) explicitly inferred the pattern of acquisition of mammalian characters in the synapsids from the cladogram of the known fossil members, and showed that it is consistent with a correlated progression. At each hypothetical stage that can be reconstructed from the morphology of a known fossil form,

characters associated with several different functions were found to have changed. On virtually every occasion these include characters associated, respectively, with locomotion and feeding, but usually others as well, such as those associated with ventilation, sense organs and brain size. For example, comparing the reconstructed hypothetical common ancestor of sphenacodontid pelycosaurs and therapsids with that of the therapsids indicates that, among others, the following evolutionary changes had occurred:

1. enlargement of the canines;
2. enlargement of the temporal fenestra and reflected lamina of the angular;
3. gracile limb bones and a facultative parasagittal gait;
4. less constrained shoulder joint;
5. reduced digit length;
6. lighter stapes indicating more acute hearing.

The transition from the common ancestor of the therocephalians plus cynodonts to the common ancestor of the cynodonts can likewise be inferred to have involved change in a variety of its functional systems, including:

1. mammalian style of tooth differentiation, including multicusped postcanines;
2. further enlargement of temporal fenestra, and coronoid process of dentary;
3. reduction of postdentary bones and quadrate, associated with enhanced high-frequency hearing;
4. nasal cavity with a more complex internal structure, associated with olfaction.
5. secondary palate;
6. enlarged brain;
7. full differentiation of vertebral column, including a basically mammalian atlas-axis;
8. enlarged ilium and reduced pubis.

These two transitions are the largest morphological shifts within the fossil record of non-mammalian synapsids. Whether this is because there really was a rapid evolutionary transition or whether it is an artefact of missing intermediate-grade fossils cannot of course be ascertained. However, Sidor & Hopson (1998) showed a surprisingly good correlation between the number of new characters at each of the nodes of their synapsid cladogram and the estimated time between the nodes, as inferred from the dates of appearance in the record of the relevant fossils. At the admittedly limited taxonomic resolution that this represents, it is consistent with a relatively constant rate of acquisition of mammalian characters, which too is what the correlated progression model would predict.

The existing synapsid fossil record is inadequate to illustrate anywhere near the full sequence of acquisi-

tion of mammalian characters, including those associated directly with endothermy, and there are many physiological characters whose evolutionary history is unlikely ever to be revealed. On the other hand, at the level of the taxonomic and organismic resolution that it does have, the fossil record is fully compatible with correlated progression. There is no anatomical evidence indicating unambiguously that any one particular function was ever the sole focus of selection at any particular time.

CONCLUSIONS

The integrated theory of the origin of endothermy presented here is that the several individually definable functions of endothermy, and the structures and processes responsible for it, all evolved in a loosely correlated progression, a small step in this structure here, a small step in that process there, and so on. As so expressed, even this is a limited view, because endothermy itself cannot be disentangled as a discrete function from its inextricable integration with all the features of the biology of the organism, as illustrated in Figure 3. Virtually everything in the biology and life of a mammal is either contributory to, or affected directly or indirectly by, the endothermic temperature strategy.

The theory reconciles the various previous theories, in the sense that each of them is regarded as partly correct. It also appears to correspond with realistic assumptions about how complex biological structure, and therefore new higher taxa that manifest it, can be expected to evolve. From this broader perspective, there are several corollaries.

1. No single, identifiable selection pressure for any one characteristic of an organism persists beyond the possible brief periods when a particular structure or function may be limiting further evolutionary change of the whole organism. Because the proposed change possible in any one characteristic at any one time is presumed always to be small, this will never be more than a transient stage, perhaps represented by a single or a few speciation events.

2. The exact pattern of small changes from the initial ancestral condition to the final derived condition will be below the resolution of any available evidence to illustrate, be it palaeontological or neontological. Therefore, the question to ask when seeking to explain a major evolutionary transition such as the origin of mammals is not, as traditionally, what particular aspect of the environment provided the selection pressure. Rather, the research programme should be focused on how the attributes of the organisms in question were functionally interrelated to one another such that a correlated progression from ancestral to descendant morphology, from original to new habitat or way of life, was possible.

3. Given the assumed loose correlation between the parts, it is easy to explain how relatively minor variations, of the kind associated with radiation at the species and genus level, can occur at every stage along the main evolving lineage. The fossil record of the synapsids illustrates this well, where radiations of a variety of differently adapted kinds of taxa occur at several levels, pelycosaur, basal therapsid and cynodont.

4. There is a degree of randomness about the evolution of individual characters. In some cases a variant of a character at any particular time may not be selected even though it would improve the efficiency of the function it directly serves. Conversely, a variant of a character may be fixed because it happens by chance to be present in what is the overall fittest phenotype, while itself being selectively neutral or even to a degree deleterious. Thus, the evolutionary pathway followed by the lineage perhaps wanders rather more aimlessly through morphospace than often supposed.

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